

ACTION OF BECKMANN'S CHROMIC ACID MIXTURE ON SOME MONOCYCLIC TERPENES

BY

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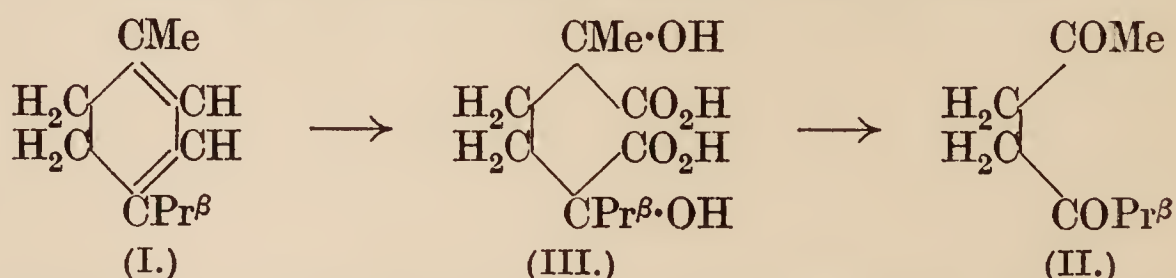
XI.—*Action of Beckmann's Chromic Acid Mixture
on Some Monocyclic Terpenes.*

By THOMAS ANDERSON HENRY and HUMPHREY PAGET.

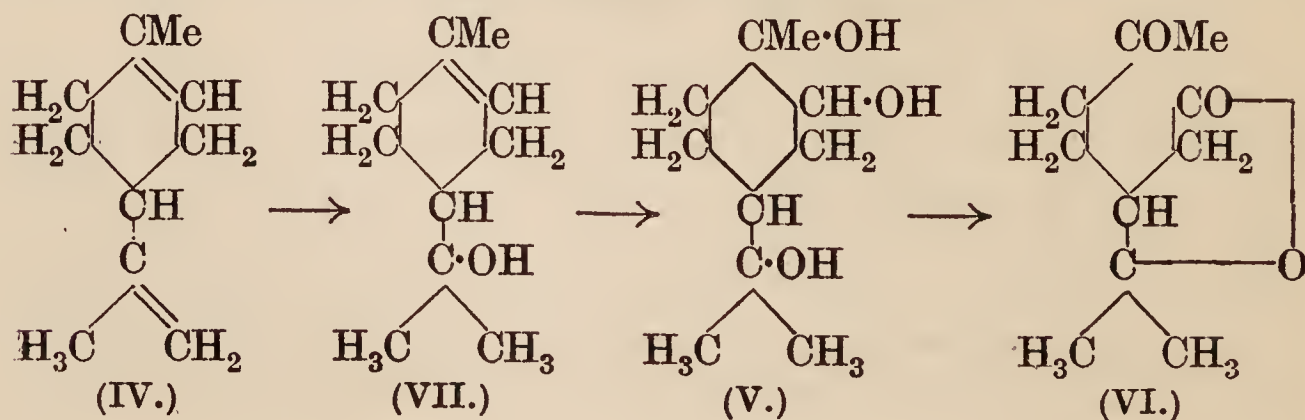
OF the fourteen possible structural isomerides which can be represented by the *p*-menthadiene formula for monocyclic terpenes, eight are known with certainty, four are doubtful, and two are unknown. There are, on the other hand, described in the literature a considerable number of natural hydrocarbons of the formula $C_{10}H_{16}$, the constants of which indicate that they may be *p*-men-

thadienes, but from which crystalline derivatives of the type used for the identification of such terpenes have not been obtained. One of these was the so-called "lævorotatory terpene of chenopodium oil," and in showing that this was composed of a mixture of α -terpinene, *l*-limonene, and *isolimonene* ($\Delta^{2:8(9)}$ -*p*-menthadiene) with *p*-cymene, the authors obtained useful confirmatory evidence by examination of the products formed by the gradual oxidation of the mixture with Beckmann's chromic acid mixture (Henry and Paget, J., 1925, **127**, 1649). As a preliminary to that work, a number of the monocyclic terpenes obtainable commercially in a reasonably pure state were oxidised with Beckmann's mixture, and the products examined. As these results, particularly those obtained with α -phellandrene, are of considerable interest and as the method may prove useful in facilitating the identification of terpenes in complex natural mixtures of these products, especially where much *p*-cymene is present, it has been thought desirable to place them on record.

It has already been shown (Henry and Paget, J., 1921, **119**, 1714; 1923, **123**, 1878) that with this oxidising agent α -terpinene (I) is converted mainly into dimethylacetylacetone (II), only minute quantities of the usual precursor of this diketone, $\alpha\delta$ -dihydroxy- α -methyl- δ -isopropyladipic acid (III), being obtained, even when the reaction is not prolonged. With potassium permanganate, on the contrary, the diketone is formed only in small amounts, the acid in its *anti*- and *para*-forms being the chief product.

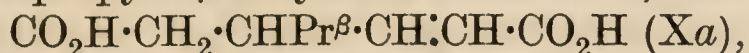


α -Terpinene is readily destroyed; but limonene (IV) is only slowly attacked by Beckmann's mixture, yielding 1:2:8-trihydroxyterpan (V), m. p. 122°, and the keto-lactone (VI) which Wallach (*Annalen*, 1893, **275**, 153) first obtained by the oxidation of α -terpineol (VII); this, therefore, is probably the product first formed by the action of chromic acid on limonene.



The α -phellandrene (VIII) used was purchased on various occasions in London and its botanical origin is unknown, although it was no doubt derived from one or other of the species used for the production of eucalyptus oil. All the samples yielded the same products on oxidation with Beckmann's mixture, *viz.*, thymoquinone and two *ketolactones*, $C_{10}H_{16}O_3$ and $C_9H_{14}O_3$, both of which were isolated in the form of their semicarbazones, which are separable from each other with great difficulty.

The keto-lactone $C_{10}H_{16}O_3$ (IX) is oxidised by sodium hypobromite, but instead of the dibasic hydroxy-acid or its lactone, which would be the normal product, a *dibasic acid*, $C_9H_{14}O_4$, is formed, which is readily oxidised further by potassium permanganate to α -isopropylsuccinic acid. Such a dibasic acid may arise from the dibasic hydroxy-acid by loss of water in two ways, to give either β -isopropyl- $\alpha\beta$ -dihydromuconic acid,

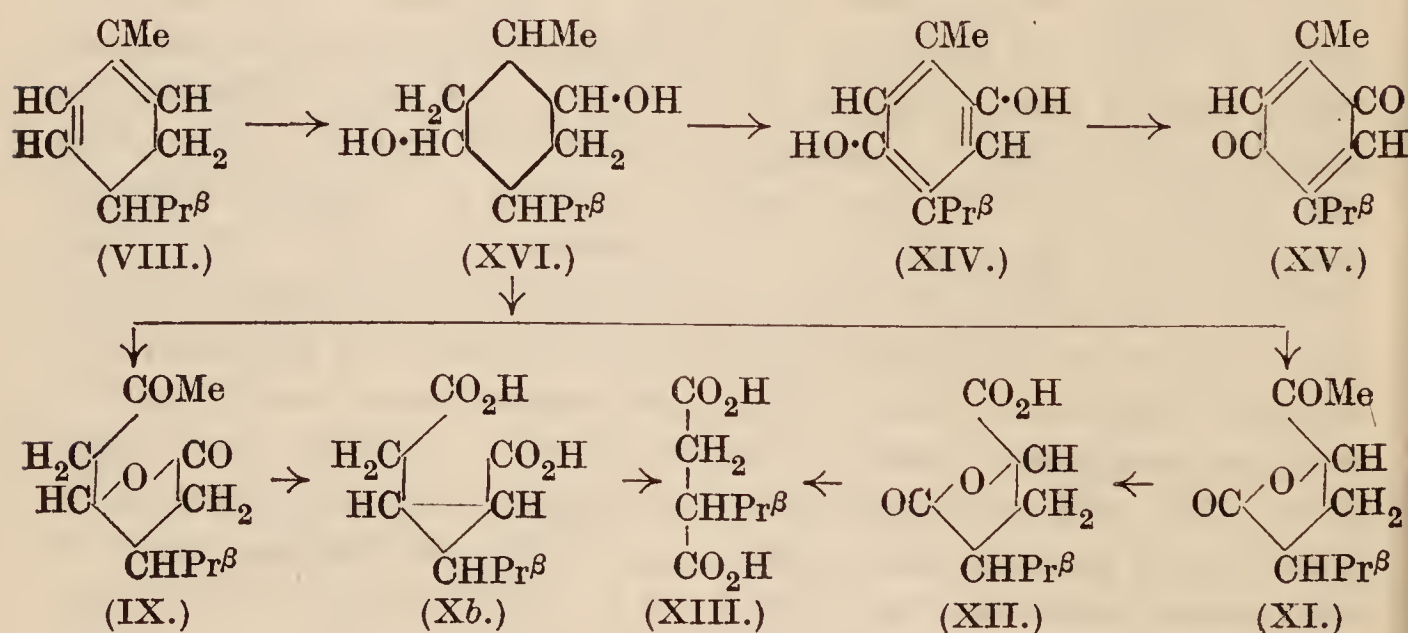


which should readily absorb bromine (compare Baeyer and Rupe, *Annalen*, 1890, **256**, 18), or, if carbon atoms 3 and 5 are involved, a *cyclopropane* derivative (Xb). Oxidation of either could give rise to isopropylsuccinic acid, being preceded in the second case by hydration, as in that of dimethyldicyclopentanonedicarboxylic acid (Farmer and Ingold, J., 1920, **117**, 1369). The molecular refraction of the diethyl ester is closer to that calculated for the unsaturated structure, on the usual assumptions (Eisenlohr, "Spectrochemie organischer Verbindungen," 1912, p. 48), than to that for the *cyclopropane* structure, but as we were unable to form any addition product with bromine the cyclic formula cannot be left out of account.

The second keto-lactone, $C_9H_{14}O_3$, we propose to represent by formula (XI). It furnishes with sodium hypobromite bromoform and a lactone acid, $C_8H_{12}O_4$ (XII), which on further oxidation by permanganate yields α -isopropylsuccinic acid (XIII). The latter also occurs, as would be expected, among the direct oxidation products of α -phellandrene by Beckmann's mixture, and it has already been obtained by Semmler (along with α -isopropylglutaric acid: the latter being attributed to the presence of β -phellandrene) by the oxidation of commercial phellandrene from eucalyptus oil with permanganate (*Ber.*, 1903, **36**, 1749). Semmler's acid had m. p. 116° , was optically active, although no specific rotation is quoted, and gave an anilic acid, m. p. 143° ; the melting point of the racemic anilic acid has been given as 145° (Bentley, Perkin, and Thorpe, J., 1896, **69**, 274), 139° (Bone and Sprankling, J., 1900, **77**, 658), and 135° (Crossley, J., 1902, **81**, 682). The acid we have obtained has m. p. 95° , $[\alpha]_D - 22.64^\circ$ (sodium salt), and yields an

anilic acid, m. p. 129° . Apart from an observation by Wallach (*Annalen*, 1900, **313**, 354), who gives $85-88^{\circ}$, no melting point lower than 115° seems to have been recorded previously for α -isopropylsuccinic acid, and we at first thought our acid must be *l*- α -isopropylglutaric acid, for which m. p.'s 92° to 97° have been recorded and from which on one occasion Wallach prepared an anilic acid, $[\alpha]_D - 24.2^{\circ}$, m. p. 129° (*Annalen*, 1911, **379**, 189), although this derivative is stated by Semmler (*loc. cit.*) to melt at 159° . To make sure of this point, we resolved *dl*- α -isopropylsuccinic acid into its optical antipodes. The two optically active forms obtained melted at 94° , and had $[\alpha]_D \pm 23^{\circ}$ (approx.). The anilic acid of the *d*-form had m. p. 129° . Mixtures of our acid with (a) the *d*-form and (b) the *l*-form melted at 117° and 94° , respectively, and a mixture of our anilic acid with that from the *d*-acid at 142° . There can be no doubt, therefore, that the acid produced directly and indirectly by the oxidation of *l*- α -phellandrene is *l*- α -isopropylsuccinic acid. In addition, a small quantity of the racemic acid was obtained, probably due to some racemisation of the *l*-phellandrene.

In view of these facts, it seems possible that occasionally α -isopropylsuccinic acid has been mistaken for α -isopropylglutaric acid. Thus in Wallach's case (*loc. cit.*) the original acid melted at $92-93^{\circ}$ and had $[\alpha]_D - 15.82^{\circ}$, but on treatment of its anhydride with aniline it yielded two anilic acids, melting at $153-155^{\circ}$ and 129° , respectively. Only the former was analysed and gave good results for isopropylglutaranilic acid. The second anilic acid had $[\alpha]_D - 24.2^{\circ}$, and it seems quite likely that it was α -isopropylsuccinanilic acid and that the acid, m. p. $92-93^{\circ}$, was a mixture.



There is also formed from α -phellandrene, in addition to these acids, thymoquinol (XIV) and thymoquinone (XV). The latter

has been found to form a disemicarbazide derivative in addition to the hydroxymethylisopropylbenzeneazoformamide described by Heilbron and Henderson (J., 1913, **103**, 1419).

The ultimate residue of unattacked oil is a mixture of cineole, which is a natural constituent of the oil from which the α -phellandrene was prepared, and *p*-cymene, which is also known to occur in the essential oils of the eucalyptus species (see Baker and Smith, "Eucalypts and their Essential Oils," 1920, p. 356); the latter was identified by analysis and by oxidation to *p*-hydroxyisopropylbenzoic acid.

That *p*-cymene was actually present in the commercial phellandrene used, was proved by removing the phellandrene as the nitrosite and the cineole as the resorcinol compound and examining the residual oil; it was then found that about 17% of the original material consisted of this hydrocarbon. *p*-Cymene is attacked exceedingly slowly by Beckmann's chromic acid mixture, yielding *p*-methylacetophenone in minute quantities.

All the oxidation products of α -phellandrene now described may be regarded as derived from a primary dihydric cyclic alcohol (XVI) produced by the addition of the elements of a molecule of water at each of the ethylenic linkages of α -phellandrene (VIII).

It is probable that this is also the chief mode of attack of the reagent on α -terpinene (I), since dimethylacetylacetone (II) is the normal product and only minute quantities of $\alpha\delta$ -dihydroxy- α -methyl- δ -isopropyladipic acid have been found, for the formation of which it is necessary to assume (Wallach, *Annalen*, 1908, **362**, 296) the addition of a hydroxyl group at each end of each of the ethylenic linkages. On the contrary, the production of 1 : 2 : 8-trihydroxyterpan (V) from limonene (IV) requires the hydration of the extracyclic ethylenic linkage to form terpineol (VII) and the subsequent addition of a hydroxyl group at each end of the cyclic double linkage to form the trihydric alcohol (V).

EXPERIMENTAL.

In the earlier experiments, 100 c.c. of the terpene under examination were shaken repeatedly with an equal volume of Beckmann's mixture until no further absorption of the terpene took place, but it was subsequently found more convenient to treat the terpene with 20 times its volume of the oxidising agent, and to submit the recovered oil to a second treatment as soon as enough had been accumulated for this purpose. Both processes yielded the same products. The unattacked oil (D) was separated from the chromic acid liquor and the latter was thoroughly extracted with ether free from alcohol. On removal of the solvent, a viscid oil was left,

which was redissolved in sufficient ether and separated into acid (B) and neutral (A) portions by repeated agitation with a saturated aqueous solution of sodium carbonate. A further quantity of acid (C) was usually obtained by concentrating the chromic acid liquor after neutralisation, again making it acid and extracting it with ether.

Limonene.

Limonene is much less readily attacked by Beckmann's mixture than phellandrene, but oxidation proceeds a little more rapidly if the terpene is diluted with an equal volume of glacial acetic acid.

Limonene ($d_{16}^{16^\circ}$ 0.8484, $[\alpha]_D^{16^\circ} + 90.1^\circ$) (50 c.c.), dissolved in glacial acetic acid (50 c.c.), was shaken mechanically for 5 days with 1000 c.c. of Beckmann's mixture. The unattacked terpene was then separated (46 c.c.) and the products were treated as described above; after 14 repetitions of the process, 8 c.c. of oil remained, $[\alpha]_D^{16^\circ} + 48.5^\circ$. The neutral extract (A) (28 g.), after distillation, yielded a *semicarbazone* which crystallised from alcohol in minute needles, m. p. 210° , $[\alpha]_D^{18^\circ} + 1.28^\circ$ in acetic acid ($c = 1.486$) (Found: C, 54.4; H, 8.0; N, 18.1. $C_{11}H_{19}O_3N_3$ requires C, 54.8; H, 7.9; N, 17.4%). This was proved by a mixed melting-point determination to be identical with the semicarbazone of the keto-lactone, $C_{10}H_{16}O_3$, obtained by the oxidation of α -terpineol. The keto-lactone, recovered as described (p. 76), had m. p. $58-60^\circ$; $[\alpha]_D^{18^\circ} - 2.12^\circ$ in water ($c = 1.552$) and -7.87° in benzene ($c = 2.008$) (Found: 1 g. equiv. to 5.31 c.c. of *N*-sodium hydroxide. Calc. for $C_{10}H_{16}O_3$, 5.4 c.c.).

The residue from the distillation of the crude extract deposited on standing a small amount of a neutral crystalline substance, insoluble in ether, with which it was well washed; it then melted at 121° , alone or mixed with a specimen of 1:2:8-trihydroxyterpan, $C_{10}H_{20}O_3$, prepared from α -terpineol by oxidation with potassium permanganate as described by Wallach (*Annalen*, 1893, 275, 153).

α -Phellandrene.

The four supplies of commercial α -phellandrene used had the following constants: $d_{16}^{16^\circ}$ 0.8525, $[\alpha]_D^{16^\circ} - 98.5^\circ$; $d_{16}^{16^\circ}$ 0.8519, $[\alpha]_D^{16^\circ} - 67.7^\circ$; $d_{16}^{16^\circ}$ 0.8828, $[\alpha]_D^{16^\circ} - 56.1^\circ$; $d_{20}^{20^\circ}$ 0.8531, $[\alpha]_D^{20^\circ} - 75.0^\circ$.

From 1 litre of terpene the average yields of the four crude oxidation products referred to above were (A) 110 g.; (B) 102 g.; (C) 28 g.; (D) 590 g.

Extract A (Neutral Oil).—This on treatment with semicarbazide acetate in alcohol yielded immediately a *semicarbazone*, crystallising in colourless, glistening leaflets, but all attempts to isolate the

original carbonyl compound from the crude extract by direct or steam distillation, or by the use of sodium hydrogen sulphite solution, failed. The total extract was therefore treated with excess of semicarbazide solution, and the mixture left for about 12 hours. The product was recrystallised until of constant melting point, 187° (corr.), from hot 95% alcohol. It had $[\alpha]_{\text{D}}^{20} + 28.9^{\circ}$ ($c = 0.26$ in alcohol or 1.96 in acetic acid), $+ 11.27^{\circ}$ ($c = 1.61$ in alcoholic sodium ethoxide), or $+ 4.13^{\circ}$ ($c = 1.6$ in aqueous sodium hydroxide) (Found for substance dried in a vacuum at 105° : C, 52.65; H, 7.7; N, 18.75. $\text{C}_{10}\text{H}_{17}\text{O}_3\text{N}_3$ requires C, 52.9; H, 7.5; N, 18.5%).

The semicarbazone was hydrolysed by 15% hydrochloric acid in presence of ether, the ethereal solution washed with sodium carbonate solution and dried over anhydrous sodium sulphate, and the solvent distilled off, leaving a colourless oil, which crystallised. It had m. p. $48-50^{\circ}$, $[\alpha]_{\text{D}}^{20} + 37.1^{\circ}$ in water ($c = 1.67$) and -43.13° in benzene ($c = 1.46$) (Found: C, 63.4; H, 8.4. $\text{C}_9\text{H}_{14}\text{O}_3$ requires C, 63.5; H, 8.2%). An aqueous solution of the substance remains neutral for several days, but such solutions neutralise caustic alkalis and 6.1 c.c. of *N*-sodium hydroxide were necessary to neutralise 1 g. of the substance. The amount of alkali required to convert a keto-lactone $\text{C}_9\text{H}_{14}\text{O}_3$ into the corresponding ketohydroxy-acid, $\text{C}_9\text{H}_{16}\text{O}_4$, is 5.9 c.c. Attempts to isolate the acid from solutions of the sodium salt by addition of weak acids and extraction with solvents merely led to the regeneration of the original keto-lactone.

The keto-lactone (0.9 g.), dissolved in the calculated quantity of *N*-sodium hydroxide, was treated with a 4% solution of potassium permanganate until decolorisation no longer took place rapidly. The oil (0.8 g.) extracted from the acidified liquor by ether had a strong odour of acetic acid and crystallised on standing. The crystals had m. p. $93-95^{\circ}$, alone or mixed with *l*-isopropylsuccinic acid prepared as described below; admixture with *d*-isopropylsuccinic acid raised the melting point to $110-117^{\circ}$.

When the keto-lactone (3 g.), dissolved in the calculated quantity of aqueous sodium hydroxide, was added to excess of a freshly-prepared, ice-cold solution of sodium hypobromite, the mixture became cloudy and deposited bromoform. After 1 hour, the latter was extracted with ether and the aqueous liquor was freed from hypobromite by cautious addition of sodium hydrogen sulphite, acidified, and again extracted with ether. This removed an oil (2.3 g.), which on careful trituration with dry benzene deposited a crystalline substance, m. p. 225° (decomp.), which contained 31% of bromine but could not be obtained in sufficient quantity for

detailed examination. The bulk of the acid was evidently a lactonic acid, since 1 g. required 6.15 c.c. of *N*-sodium hydroxide for neutralisation in the cold and 10.74 c.c. when heated with the alkali ($C_8H_{12}O_4$ requires 5.8 c.c. of *N*-sodium hydroxide for neutralisation of one carboxyl group and 11.65 c.c. for conversion into the corresponding hydroxy-dicarboxylic acid $C_8H_{14}O_5$). The *silver* salt prepared from the disodium salt contained Ag, 53.6% (Calc. for $C_8H_{12}O_5Ag_2$: Ag, 53.4%) (Found for *lead* salt: C, 24.9; H, 3.7; Pb, 52.3. $C_8H_{12}O_5Pb$ requires C, 24.3; H, 3.0; Pb, 52.4%).

On regeneration from the lead salt by treatment with dilute sulphuric acid and extraction with ether, the original lactonic acid was obtained as an oil, which slowly solidified when kept in a vacuum desiccator; it then melted at 58—60° (Found: C, 55.75; H, 7.0. $C_8H_{12}O_4$ requires C, 55.9; H, 7.0%).

On further oxidation with potassium permanganate, this lactonic acid, $C_8H_{12}O_4$, was converted into *l*-isopropylsuccinic acid, which was isolated and identified as described above (p. 76).

This stage of the oxidation of α -phellandrene is represented by formulæ VIII, XVI, XI, XII and XIII (p. 73).

On keeping the liquors from which the semicarbazone, m. p. 187°, was separated, for 2—3 days, a second semicarbazone was obtained the yield of which varied from a mere trace to as much as 20%. It crystallised from alcohol in small, colourless needles, m. p. 183°, $[\alpha]_D^{21} + 55.47^\circ$ in acetic acid ($c = 2.08$) (Found: C, 54.8; H, 8.0; N, 17.8. $C_{11}H_{19}O_3N_3$ requires C, 54.8; H, 7.9; N, 17.4%). A mixture with the first semicarbazone melted at 168—174°. The solubility of these two semicarbazones in alcohol is about the same, 0.2% at 15°; a mixture of the two is more soluble and very difficult to separate.

The carbonyl compound was obtained from the semicarbazone by the method already described (p. 76). It did not crystallise but distilled unchanged at 155—160°/1 mm.; $[\alpha]_D^{20} + 73.67^\circ$ in water ($c = 1.775$) and $+ 54.79^\circ$ in benzene ($c = 1.566$) (Found: C, 65.1; H, 9.0. $C_{10}H_{16}O_3$ requires C, 65.2; H, 8.7%). It dissolves to a neutral solution in water, but this solution neutralises sodium hydroxide, 1 g. of the substance requiring 5.36 c.c. of *N*-sodium hydroxide ($C_{10}H_{16}O_3$ requires 5.44 c.c. for conversion into the ketohydroxy-acid, $C_{10}H_{18}O_4$). The substance is therefore a *keto-lactone*, $C_{10}H_{16}O_3$.

When this keto-lactone (1.7 g.) was oxidised with alkaline hypobromite as described above, bromoform was produced and an almost quantitative yield (1.5 g.) was obtained of an *acid* which after recrystallisation from benzene melted constantly at 138° and had $[\alpha]_D^{19} + 15.99^\circ$ in aqueous sodium hydroxide ($c = 4.196$). It was

readily soluble in alcohol or ether, sparingly soluble in water. It gave no evidence of a lactone structure (Found: C, 58.0; H, 7.6. 1 G. was equiv. to 10.58 c.c. of *N*-sodium hydroxide. Found in the silver salt: Ag, 53.6. $C_9H_{14}O_4$ requires C, 58.1; H, 7.6%. 1 G. is equiv. to 10.74 c.c. of *N*-sodium hydroxide. $C_9H_{12}O_4Ag_2$ requires Ag, 53.95%). The diethyl ester distilled at 168—170°/17 mm. and had d_{19}^{19} 1.0046, $[\alpha]_D^{18} + 18.05^\circ$ in alcohol ($c = 7.26$), n_D^{20} 1.4530, whence $[R_L]_D = 65.15$ (Found: C, 64.1; H, 9.25. $C_{13}H_{22}O_4$ requires C, 64.5; H, 9.1%). The calculated molecular refraction for a diethyl ester of this empirical formula is 63.11, to which must be added 1.73 for an ethylenic linkage or 0.7 for a cyclopropane structure, making 64.84 and 63.81, respectively. It was therefore a dicarboxylic acid and appeared not to contain an ethylenic linkage, since on treatment with bromine in solvents no addition took place and the acid was recovered unchanged; the ester behaved similarly. The acid was readily oxidised by an aqueous solution of potassium permanganate at 0°, yielding an *acid* which slowly crystallised in plates, m. p. 95°, and showed no depression of melting point when mixed with *l*-isopropylsuccinic acid, but raised that of the *d*-acid to 113—117°. This stage of the oxidation of α -phellandrene is represented by formulæ VIII, XVI, IX, Xa or Xb, XIII (p. 73).

Extracts B and C.—The acid extracts did not crystallise on standing; an insoluble lead salt was obtained by addition of lead acetate to an aqueous solution of the acids, previously neutralised by sodium hydroxide. The acid recovered from this lead salt crystallised from water, in which it was very soluble, in plates, m. p. 95°; $[\alpha]_D^{18} - 22.64^\circ$ in water ($c = 8.80$) [Found: C, 52.9; H, 7.7. 1 G. was equiv. to 11.8 c.c. of *N*-sodium hydroxide. $C_5H_{10}(CO_2H)_2$ requires C, 52.5; H, 7.5%. 1 G. is equiv. to 12.5 c.c. of *N*-sodium hydroxide]. The anhydride distilled at 140—150°/15 mm., and with aniline in benzene solution gave an *anilic acid* crystallising from benzene in leaflets, m. p. 129° (Found: N, 6.1. $C_{13}H_{17}O_3N$ requires N, 5.9%). *dl*-isoPropylsuccinic acid melts at 117° and its anilic acid at 144°, and admixture of these substances caused no depression of melting point below those of the acid and anilic acid, respectively, from phellandrene, which therefore appeared to be *l*-isopropylsuccinic acid and its anilic acid. Since some confusion exists as to the physical constants of the optically active forms of this acid (see p. 73), and it appears unlikely that it has previously been obtained in a pure state, a specimen of the *dl*-acid, m. p. 117°, $[\alpha]_D \pm 0^\circ$, the remainder of a sample received from the late Prof. A. W. Crossley, was resolved. The *quinine* salt crystallised well from alcohol, the less soluble salt (m. p. 206°, $[\alpha]_D^{25} - 125.4^\circ$) yielding an acid, m. p. 93—105°, $[\alpha]_D^{20} + 12.1^\circ$.

The *quinidine* salt also crystallised well, but, like the *quinine* salt, only furnished a partly deracemised acid. The *strychnine* salt separated from alcohol in long needles. On drying in a vacuum at 100° , or on boiling with alcohol, this salt partly dissociated and free *strychnine* was obtained as a first crop, $[\alpha]_{\text{D}}^{25} - 140.9^{\circ}$ in chloroform ($c = 1.884$). The second crop also contained free *strychnine*, and no accurate constants could be obtained for the salt. From the second and other early fractions, however, an acid was recovered, m. p. 94° , $[\alpha]_{\text{D}}^{20} + 22.99^{\circ}$ in water ($c = 5.64$). When no more of the sparingly soluble *strychnine* salt could be induced to separate, the acid was recovered from the residues and converted into the *brucine* salt, which crystallised well from acetone; m. p. 144° (decomp.), $[\alpha]_{\text{D}}^{20} - 15.9^{\circ}$ in chloroform ($c = 1.929$). The acid recovered from this melted at 94° and had $[\alpha]_{\text{D}}^{20} - 23.46^{\circ}$ in water ($c = 12.866$). This *l*-acid showed no depression of melting point when mixed with the *l*-acid, $\text{C}_7\text{H}_{12}\text{O}_4$, obtained directly (p. 78) and indirectly (p. 76) from *phellandrene*; admixture with the *d*-acid raised the melting point to $115\text{--}117^{\circ}$, and this was not depressed by further addition of the *dl*-acid. The anilic acid prepared from the anhydride of the *d*-acid obtained by distillation melted at 129° , and a mixture of this with the anilic acid of the *l*-acid from *phellandrene* at $142\text{--}144^{\circ}$.

The remainder of the extracts B and C consisted of oily acids from which no well-defined product could be isolated, either by fractional precipitation with metallic salts or by fractional distillation of the ethyl or methyl esters.

Recovered Oil (D).—The colour of the unoxidised oil varied from pale yellow to dark brown. It was separated by distillation into four fractions: (1) b.p. $70^{\circ}/25$ mm. or $172\text{--}180^{\circ}/760$ mm. (60%); (2) b. p. $70\text{--}110^{\circ}/25$ mm. (25%); (3) b. p. $115\text{--}120^{\circ}/25$ mm. (8%); and (4) a black, tarry residue, distilling with decomposition at $200^{\circ}/15$ mm. (7%).

Fraction (1) had a strong odour of cineole, due, no doubt, to the presence of this substance in the *phellandrene* used, and cineole equivalent to 8% by weight of extract D was isolated from it by repeated agitation with a 50% solution of resorcinol. The residue of fraction (1), after removal of cineole and repeated distillation over metallic sodium, had b. p. $176\text{--}180^{\circ}/760$ mm., $[\alpha]_{\text{D}} \pm 0^{\circ}$, and consisted principally of *p*-cymene, identified by oxidation to hydroxy-isopropylbenzoic acid, m. p. 157° , with a hot aqueous solution of potassium permanganate. The yield of *p*-cymene amounted to about 25% of the α -*phellandrene* used. An attempt to estimate the amount of *p*-cymene originally present was made by removing the *phellandrene* as nitrosite in the way described by Smith, Hurst,

and Read (J., 1923, **123**, 1663). The petroleum solution from which the nitrosite was removed was again treated with nitrous acid, and the residual oil then shaken three times, for several hours at a time, with a 50% solution of resorcinol in water, and finally repeatedly distilled over sodium at 176—178°/760 mm. The amount of *p*-cymene remaining was 17% (Found: C, 89.5; H, 10.5. Calc.: C, 89.55; H, 10.45%).

Fractions (2) and (3) were bright yellow to brown and on standing for some time with an alcoholic solution of semicarbazide acetate deposited either yellow crystals, or colourless crystals which rapidly became yellow on exposure to light. Both forms melted at temperatures varying from 224° to 237° and on recrystallisation from boiling acetic acid gave bright yellow fractions melting constantly at 237°; a second yellow crystalline substance, which melted constantly at 204°, accumulated in the acetic acid mother-liquors. A similar but less complete separation can be effected by boiling alcohol, in which the substance melting at 237° is much less soluble than in acetic acid, but treatment with boiling alcohol leaves undissolved a minute amount of a pale yellow substance, m. p. 257°.

The substance melting at 204° appears to be the 4-hydroxy-3-methyl-5-isopropylbenzeneazoformamide of Heilbron and Henderson (*loc. cit.*) formed by the interaction of thymoquinone with one molecule of semicarbazide. It separates from acetic acid in bright red crystals, which rapidly effloresce and become yellow, losing two molecules of acetic acid on exposure at room temperature. Dried at 100° in a vacuum, it lost 35.5% ($C_{11}H_{15}O_2N_3$, $2C_2H_4O_2$ requires loss, 35.2%) (Found: C, 59.6; H, 6.9; N, 19.0. $C_{11}H_{15}O_2N_3$ requires C, 59.7; H, 6.8; N, 19.0%).

The yellow and the white substance melting at 237° appear to be two forms of *thymoquinone disemicarbazone* (Found: C, 51.7; H, 6.8; N, 29.9. $C_{12}H_{18}O_2N_6$ requires C, 51.8; H, 6.5; N, 30.2%). This has never been prepared previously, but can readily be obtained by the action of excess of semicarbazide acetate on thymoquinone dissolved in cymene or any other solvent which will retard reaction between the two components, or by prolonged ebullition of thymoquinone with excess of semicarbazide in alcohol. Under these conditions, the yellow form, m. p. 237°, alone is produced (Found: N, 29.9%). We have been unable to determine the conditions which will lead with certainty to the production of the labile white form, but once it is produced it can be preserved by washing it with cold acetic acid and storing it in the dark. On recrystallisation from boiling acetic acid, both this colourless form and the substance melting at 257° pass into the yellow modification, m. p. 237°.

Fraction (4), on long standing and careful trituration with ether,

deposited a small amount of a colourless, crystalline substance, m. p. 142° , which proved to be thymoquinol, since it showed no depression of melting point when mixed with thymoquinol prepared by reduction of thymoquinone with titanous chloride (Found: C, 72.1; H, 8.7. Calc. for $C_{10}H_{14}O_2$: C, 72.3; H, 8.4%).

The remainder of fractions (2), (3), and (4) consisted of oily and tarry substances from which no well-defined products could be isolated.

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